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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/716,166	11/17/2000	Douglas A. Treco	10278-014001	6951

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FISH & RICHARDSON PC
225 FRANKLIN ST
BOSTON, MA 02110

EXAMINER
JIANG, DONG

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/09/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/716,166	TRECO ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cov r sheet with th correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-17,19 and 21-93* is/are pending in the application.

4a) Of the above claim(s) *16 and 53-82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-15,17,19,21-52 and 83-93* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-6,8-17,19 and 21-93* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to comply (sequence)* .

DETAILED OFFICE ACTION

Applicant's amendment in paper No. 13, filed on 24 June 2003 is acknowledged and entered. Following the amendment, claims 7, 18 and 20 are canceled, claims 1-6, 8-10, 14, 15, 17, 19, 26-28, 31, 32, 34, 41, 45, 47, 51, 52 and 83 are amended, and the new claims 84-93 are added.

Currently, claims 1-6, 8-17, 19, and 21-93 are pending, and 1-6, 8-15, 17, 19, 21-52 and 83-93 are under consideration.

Withdrawal of Objections and Rejections:

All objections and rejections of claims 7, 18 and 20 are moot as the applicant has canceled the claims.

The objection of claims 1, 5, 28, 34 and 52 is withdrawn in view of applicant's amendments.

The prior art rejection of claims 1-4, 6-10, 12, 14, 17-20, 22, 23, 26-30, 32-34, 38-41, and 43-45 under 35 U.S.C. 102(b) as being anticipated by Sevarino et al. (Cell, 1989, 57(1): 11-19) is withdrawn in view of applicant's amendment.

The prior art rejection of claim 5, 9, 11, 13, 31, 35, 37, 46, 52 and 83 under 35 U.S.C. 103(a) as being unpatentable over Sevarino et al. (Cell, 1989, 57(1): 11-19), and further in view of Stoller et al. (J. Cell Biol., 1989, 108: 1647-55, provided by applicants), Habener et al. (US 5,118,666), Suzuki et al. (US 5,891,671), and Patel et al. (CIBA Foundation Symposium, 1995, 190: 26-50), is withdrawn in view of applicant's amendment, however, the amendment necessitated new art rejections set forth below.

Formal Matters:

Sequence compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

APPLICANT IS REQUIRED TO COMPLY WITH THE SEQUENCE RULES, 37 C.F.R.. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Title

The title of the invention remains not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are directed.

Claims

Claims 32 and 36 are objected to as being dependent upon a canceled claim. The applicant is required to amend the claims in independent form including all of the limitations of the base claim, or depending from an elected pending claim.

Objections and Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 8-15, 17, 19, 21-46 and 83 remain rejected, and the new claims 90-93 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 14 are indefinite for the recitation of "variant thereof which ...". It is unclear whether said variant is a variant of the pro-region of a somatostatin, or a variant of a functional fragment. The claim is further indefinite because it is unclear whether "which" refers to the functional fragment or the variant. "Which" is suggested to be replaced by language such as "wherein the variant of the pro-region of a somatostatin differs from the wild-type amino acid sequence by ..." (claim 90, for example). The claims are further

indefinite for the recitation of "a functional fragment". It is unclear what function is indicated, as the claim does not specify such, and the functional properties of the pro-region of a somatostatin are not completely clear, and it may have more than one function. As such, the metes and bounds of the claim cannot be unambiguously determined.

Claim 83 is indefinite for the recitation of "a functional fragment" for the same reason above.

Claim 36 remains indefinite for the recitation of "*the* cleavage site " in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 19 and 39 remain indefinite for the recitation of "mature form", for the reasons set forth in the last Office Action, paper No. 11, mailed on 18 December 2002, at page 4.

Applicants argument, filed on 24 June 2003 (paper No. 13) has been fully considered, but is not deemed persuasive for reasons below.

At page 18 of the response, the applicant argues that it would be clear to an ordinary skilled artisan guided by the specification that the "mature form" of the small heterologous small peptide is the small peptide having been cleaved from the pro-somatostatin sequence, which is indicated in the specification. This argument is not persuasive because the support in the specification, as applicants pointed out, merely is "preferred embodiment" or examples, which fall within the intended definition, but is not considered, in itself, to provide a definition of "mature form". The metes and bounds of the "mature form" in the claims still cannot be unambiguously determined.

Claim 27 is indefinite for the recitation of "the cell ..., further comprising at least one regulatory sequence". It is unclear what is the relationship between the regulatory sequence and the nucleic acid encoding the fusion protein, and whether the regulatory sequence is a part of said nucleic acid, and if not, how the regulatory sequence works to facilitate expression of the fusion protein.

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15, 47, and the dependent claims 48-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claim 15 is directed to a non-endocrine cell for secreting a small peptide, wherein the cell comprises a nucleic acid encoding a fusion protein comprising a signal peptide, a pro-region of a somatostatin, and a small peptide *other than somatostatin*, wherein the small peptide portion of the fusion protein is encoded by an *endogenous* genomic sequence; and a method of making said cell, wherein, by homologous recombination, the *exogenous* nucleic acid encoding the *pro-region* of a somatostatin is linked to a nucleic acid encoding the small peptide within the genome of the cell.

The specification discloses a recombinant cell transfected with a construct comprising nucleic acid encoding the prepro-region of a somatostatin and a small peptide such as GLP-1. The specification provides no instruction/guidance, nor working example as to how to make a cell wherein the exogenous nucleic acid encoding the *pro-region* of a somatostatin is linked to an endogenous genomic nucleic acid encoding the small peptide other than somatostatin.

Applicants argument in the paragraph bridging pages 19 and 20 of the response (paper No. 13) is noted, which indicates that the claim is enabled if an ordinary skilled artisan can make and use the claimed cell without undue experimentation, and a working example is not required to enable the claim, that the specification provides art-recognized methods of making the claimed cells (references cited), i.e. homologous recombination technology, which was used for making therapeutic products at the time of filing. This argument has been fully considered, but is not deemed persuasive for the following reasons.

While the Examiner acknowledges that a working example is not required to enable the claim, and the prior art has examples of homologous recombination, the instant invention does not seem achievable by applying the art-recognized methods of homologous recombination, such as those disclosed in the patents cited by applicants because: homologous recombination happens between sequences sharing sequence homology. For example, in the cited reference by applicants, US 5,641,670, Treco discloses a homologously recombinant cell for gene therapy, and a method of making thereof. Treco's recombinant cell is achieved by transfecting a cell with a construct comprising two targeting sequences homologous to hEPO gene sequence, with an insertion of an exogenous regulatory region for altering gene expression, the mMT-1. Homologous recombination occurs between the hEPO sequences in the construct and the hEPO sequence in the genome of the cell, and it occurs at a *preselected site*. The resulting cell is able to produce hEPO, which is not expressed in the untransfected counterpart. However, such is not the case in the instant invention, in which the targeting sequence seems to be that encoding for the pro-region of a somatostatin. As such, homologous recombination would occur between the exogenous sequence encoding for the pro-region of a somatostatin and the endogenous genomic sequence encoding for the pro-region of the somatostatin. Such a homologous recombination would not result in directing an expression of any small peptide, but somatostatin. Therefore, in the absence of instruction/guidance, or working example, a skilled artisan would not know how to make the claimed cell secreting a small peptide other than somatostatin because the prior art teachings do not apply in the instant situation. Undue experimentation would be required prior to practicing the claimed invention.

Claim 47 does not require the secreted small peptide to be that other than somatostatin, and thus encompass small peptides other than somatostatin, as well as somatostatin itself. The claim is not enabled with respect to the embodiment directed to the small peptide other than somatostatin for the same reasons above. Further, the claim is not enabled with respect to the embodiment directed to somatostatin because the exogenous targeting sequence of the present invention is merely a nucleic acid encoding the pro-region of a somatostatin, which sequence is already present in the genome. Additionally, the prior art has not established that this region can act as a regulatory element altering gene expression in a cell not normally expressing somatostatin. Therefore, it is unlikely that the replacement of the endogenous sequence encoding

the pro-region of preprosomatostatin with an exogenous nucleic acid having the same or similar sequence would turn a non-endocrine cell into a cell secreting somatostatin. Therefore, in the absence of instruction/guidance, or working example from the present specification, a skilled artisan would not know how to use the claimed method to make the cell secreting somatostatin. Undue experimentation would be required prior to practicing the claimed invention.

Due to the large quantity of experimentation necessary to determine how to use the claim method to make the cell of the present invention; the lack of direction/guidance presented in the specification regarding same; the absence of working examples directed to same; the complex nature of the invention; the state of the prior art which has not established that homologous recombination of specific sequences may result in expression of unrelated genes, and that the pro-region of preprosomatostatin has a regulatory effect on altering gene expression; and the breadth of the claim which embraces expression of any small peptide other than somatostatin, undue experimentation would be required of the skilled artisan to use the claimed invention.

Claim 15 remains further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons set forth in the last Office Action, paper No. 11, at pages 5-6.

Applicants argument, filed on 24 June 2003 (paper No. 13) has been fully considered, but is not deemed persuasive for reasons below.

At page 21 of the response, the applicant argues that the present invention lies in the novel way that *known and readily available* sequences are specifically selected and arranged in the claimed construct, cell and methods, and that the claimed cell is amply described, such as being a homologously recombinant cell, containing known and readily available sequences having a particular and specific arrangement, showing that applicant was in possession of the invention. This argument is not persuasive for the following reasons. Although claim analyses for the issues of enablement and written description are different, and reduction to practice is not required to meet written description requirement, in the instant case, since a skilled artisan

would not be able to make the claimed invention for the reasons above, one cannot readily envision the claimed cell based on the characteristics disclosed in the specification. As the disclosure does not enable one skilled in the art to make the claimed cell, and the lack of reduction to practice, applicants are not in possession of the claimed invention.

Claim 83 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim recites "*analog thereof*", which reads on a functional equivalent of the pro-region of a somatostatin. Such a analog may or may not have structural similarity to that of a somatostatin as there is no sequence limitation associated with the "analog". However, the specification merely discloses the use of the pro-region of a somatostatin, and there is no such analog meeting the limitations of the claim identified or particularly described in the specification .

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of the pro-region of a somatostatin, the skilled artisan cannot envision the detailed chemical structure of the encompassed analogs thereof, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to

lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, no analog of the pro-region of a somatostatin meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6 and 8-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sevarino et al. (Cell, 1989, 57(1): 11-19), in view of Stoller et al. (J. Cell Biol., 1989, 108: 1647-55, provided by applicants), Habener et al. (US 5,118,666), Suzuki et al. (US 5,891,671), and Patel et al. (CIBA Foundation Sumposium, 1995, 190: 26-50).

The teachings of Sevarino, Stoller, Habener, Suzuki, and Patel are reviewed in the last Office Action, paper No.11, and briefly reiterated below.

Sevarino discloses a vector (page 16, the right column, and page 18, the left column) for the expression of a hybrid protein, which comprises the leader sequence and a portion of the pro-

region of the rat preprosomatostatin (rPPSS) and a small heterologous peptide, which is the carboxyl terminal portion of the anglerfish preprosomatostatin-2 (a(II)PPSS). Sevarino further teaches when transfected cells with said vector, a mature form the small peptide was produced. Further, Sevarino teaches (page 16, the right column) transfected cells (AtT20 and RIN 5F) with said vector, a method of making a small peptide by culturing the transfected cells, which produce mature somatostatin peptide, and a method of making a cell expressing the small peptide by transfecting said cells with the nucleic acid construct.

Sevarino does not teach that the small peptide is one other than somatostatin.

Stoller teaches an expressing vector comprising nucleic acid sequences encoding the prepro-region of a preprosomatostatin and a heterologous polypeptide α-globin, when transfecting cells with said vector, "mature" α-globin was produced by these cells (the abstract, and page 1648, the right column), and that the chimeric polypeptide was recognized by the processing enzymes nearly as efficiently as native preprosomatostatin (page 1652, the left column), indicating the role of the pro-region of preprosomatostatin in targeting a peptide to regulated secretory pathway.

Habener teaches that GLP-1 (like somatostatin) is a peptide hormone and generated from a prohormone precursor proglucagon (column 2, lines 16-22), and that GLP-1 has insulinotropic activity, and a potential therapeutic use for diabetes mellitus (the abstract).

Suzuki teaches that it is desirable in the art to utilize the expression of a chimeric protein for a number of peptide production, and that enzymatic cleavage can be used for separating a target peptide (column 1, lines 15-18). Further, Suzuki teaches a construct for the expression of a chimeric peptide such as peptide hormones including GLP-1 (column 5, lines 13-22). Additionally, Suzuki teaches that when a peptide hormone or a precursor thereof is produced in an organism, a precursor polypeptide for the peptide is specifically cleaved by a processing enzyme such as prohormone enzyme PC1/3 and furin, and that when these processing enzymes are used for excising a target peptide from the chemeric protein, it is expected that the peptide hormone is not damaged and the processing enzyme is applicable to a wide variety of peptides, therefore, the development of such production methods has been desired in the art (column 1, lines 36-49).

Patel teaches that the mammalian pro-protein convertases comprise furin, PACE4 and PC1-6, which mediate endoproteolysis of prohormone precursors, and that furin is capable of monobasic processing prohormone precursors, such as prosomatostatin (the abstract).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to make a construct for the purpose of expressing a small hormone peptide such as GLP-1, wherein the construct comprises the nucleic sequences encoding pre- pro-regions of preprosomatostatin, a furin cleavage site, and GLP-1 as taught by Sevarino and Stoller that the pro-region of preprosomatostatin can be used for targeting a heterologous peptide to regulated secretory pathway, and by Suzuki that a chimeric prohormone of GLP-1 can be cleaved to produce the mature hormone peptide by processing enzymes such as furin. The person of ordinary skill in the art would have been motivated to make the construct and the host cell for expressing GLP-1 because of the potential therapeutic application of GLP-1 in treating diabetes as suggested by Habener, the advantage of using the pro-region of prosomatostatin in targeting the hormone peptide as taught by Sevarino and Stoller, and the advantage of using the prohormone processing enzymes such as furin for cleaving the chimeric peptide in order to remain the peptide undamaged as taught by Suzuki, and reasonably would have expected success because Sevarino and Stoller have demonstrated successful expression of two different heterologous peptides by using fusing pro-region of prosomatostatin with the target peptide, and the prior art has established that when a processing enzyme such as furin is used for excising a target peptide from the chemeric protein, the peptide hormone is not damaged, as indicated by Suzuki.

Claims 14, 17, 19, 21-35, 37-46, and 83-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sevarino et al. (Cell, 1989, 57(1): 11-19), and in view of Stoller et al. (J. Cell Biol., 1989, 108: 1647-55, provided by applicants), Habener et al. (US 5,118,666), Suzuki et al. (US 5,891,671), and Patel et al. (CIBA Foundation Sumposium, 1995, 190: 26-50), as applied to claims 1-6 and 8-13 above, and further in view of Warren et al. (Cell, 1984, 39(3 Pt2): 547-55), and Selden et al., US 6,531,124 B1.

The teachings of Sevarino, Stoller, Habener, Suzuki, and Patel are reviewed in the last Office Action, paper No.11, and above. None of them teaches recombinant expression of a small peptide such as GLP-1 in a non-endocrine cell, a non-endocrine primary cell, a non-endocrine human cell, or a fibroblast as claimed.

Warren discloses a recombinant method of making a cell for secreting somatostatin, wherein the untransfected counterpart does not normally secrete polypeptide hormones, such as COS-7 cell (the abstract). Warren teaches that gene transfection of angler fish preprosomatostatin results in the expression, proper proteolytic process, and secretion of the somatostatin (the abstract), indicating that the prepro-region of preprosomatostatin functions properly as it does in a cell naturally expressing somatostatin.

Selden discloses a recombinantly transfected primary or secondary cell for expressing hormone peptides such as EPO and GLP-1, and a method of making such a cell, and indicates that such cells are useful in methods of gene therapy (the abstract) for individuals such as diabetes patients. Further, Selden demonstrates that the transfected human primary or secondary cells, including fibroblast, efficiently express and secret the encoded peptide, EPO or GLP-1 (Examples 4, 5, 11 and 12).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to make a host cell as described in the claims for the purpose of expressing a small hormone peptide such as GLP-1, following teachings of Sevarino, Stoller, Habener, Suzuki, and Patel, wherein the cell is a non-endocrine cell as taught by Warren that a prepro-region of preprosomatostatin can functional properly as to expressing, processing, and secreting the directed peptide, such as somatostatin, in a non-endocrine cell; and to use a non-endocrine cell, such as a primary cell, a human cell, or a fibroblast as suggested by Selden. The person of ordinary skill in the art would have been motivated to make such a non-endocrine cell for expressing GLP-1 because of the potential therapeutic application of GLP-1 in treating diabetes as suggested by Habener, and for specific gene therapy using primary, human or fibroblast cell as taught by Selden, the advantage of using the pro-region of prosomatostatin in targeting the hormone peptide as taught by Sevarino and Stoller, and the advantage of using the prohormone processing enzymes such as furin for cleaving the chimeric

peptide in order to remain the peptide undamaged as taught by Suzuki, and reasonably would have expected success because Sevarino and Stoller have demonstrated successful expression of two different heterologous peptides by using fusing pro-region of prosomatostatin with the target peptide; Warren has demonstrated successful expression of somatostatin by transfecting preprosomatostatin gene into a non-endocrine cell; Selden has demonstrated successful expression of GLP-1 in a non-endocrine cell, such as a non-endocrine primary cell, a non-endocrine human cell, or a fibroblast; and the prior art has established that when a processing enzyme such as furin is used for excising a target peptide from the chimeric protein, the peptide hormone is not damaged, as indicated by Suzuki.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Dong Jiang, Ph.D.
Patent Examiner
AU1646
12/4/02

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600